

What is claimed is:

1. A method of determining whether a subject is at increased risk for alcoholism, said method comprising:

(a) administering to a subject a therapeutically effective amount of a GABA<sub>A</sub> receptor modulator and determining whether the subject is sensitive or insensitive to such GABA<sub>A</sub> receptor modulator;

(b) subsequently administering a therapeutically effective amount of a GABA<sub>A</sub> receptor agonist and determining whether the subject is sensitive or insensitive to such GABA<sub>A</sub> agonist; and

(c) correlating a decreased sensitivity to a GABA<sub>A</sub> receptor modulator and an increased sensitivity to a GABA<sub>A</sub> agonist with an increased risk of alcoholism in the subject.

2. The method of claim 1 wherein the GABA<sub>A</sub> receptor modulator is a benzodiazepine.

3. The method of claim 1 wherein the GABA<sub>A</sub> receptor agonist is gaboxadol or THIP.

4. The method of claim 2 wherein the benzodiazepine is Valium (diazepam), Activan (lorazepam), Midazolam, or Flunitrazepam.

5. The method of claim 4 wherein the dose range is from about 5 to about 20 mg.

6. The method of claim 3 wherein the dose range is from about 1 to about 3 mg/kg.

7. A method of screening for a drug which decreases expression of the  $\alpha\beta_2\delta$  subunit of GABA<sub>A</sub>, said method comprising:

- (a) isolating and culturing neurons;
- (b) applying a drug to the cultured neurons;
- (c) measuring the level of  $\delta$  subunit of GABA<sub>A</sub> from the treated neurons of step (b);
- (d) determining whether the drug applied in step (b) decreases expression of the  $\delta$  subunit of GABA<sub>A</sub> receptors; and
- (e) correlating a decrease in expression of the  $\delta$  subunit of GABA<sub>A</sub> receptors found in the treated neurons of step (b) when compared to a control neuron culture having no drug application, with the identification of a drug which decreases expression of  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors.

8. A method of screening for a drug which decreases expression of the  $\alpha_4\beta_2\delta$  subunit of GABA<sub>A</sub> receptor, said method comprising: (a) expressing  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors in eukaryotic cells; (b) applying a drug to the eukaryotic cells of (a); (c) measuring the level of  $\delta$  subunit of GABA<sub>A</sub> from the treated eukaryotic cells of step (b); (d) determining whether the drug applied in step (b) decreases expression of the  $\delta$  subunit of GABA<sub>A</sub> receptors; and (e) correlating a decrease in expression of the  $\delta$  subunit of GABA<sub>A</sub> receptors found in the treated eukaryotic cells of step (b) when compared to a control eukaryotic cell population having no drug application, with the identification of a drug which decreases expression of  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors.

9. A drug that decreases expression of the  $\alpha_4\beta_2\delta$  subunit of GABA<sub>A</sub> and identified by the method of claim 7 or 8.

10. A method of treating a subject at risk for alcoholism, said method comprising administering a therapeutically effective amount of a drug of claim 7, 8, or 9.

11. A method for identifying a drug which blocks  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors, said method comprising:

- (a) isolating and culturing neurons;
- (b) applying a drug to the cultured neurons of (a);
- (c) measuring GABA<sub>A</sub> gated currents at  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors in the treated neurons of (b); and
- (d) correlating a decrease in GABA<sub>A</sub>-gated currents recorded at  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors when compared to a control culture with no drug application, with the identification of a drug which blocks  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors.

12. A method for identifying a drug which blocks  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors, said method comprising (a) expressing  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors in eukaryotic cells ; (b) applying a drug to the eukaryotic cells of (a); (c) measuring GABA<sub>A</sub> gated currents at  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors in the treated eukaryotic cells of (b); and (d) correlating a decrease in GABA<sub>A</sub>-gated currents recorded at  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors when compared to a eukaryotic cell population having no drug application, with the identification of a drug which blocks  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors.

13. A drug which blocks  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors and identified by the method of claim 10, 11, or 12.

14. A method of treating a patient at risk for alcoholism, said method comprising administering a therapeutically effective amount of the drug of claim 11, 12 or 13.

15. A method of determining whether a subject is at increased risk for premenstrual anxiety, said method comprising:

(a) administering to a subject a therapeutically effective amount of a GABA<sub>A</sub> receptor modulator and determining whether the subject is sensitive or insensitive to such GABA<sub>A</sub> receptor modulator;

(b) subsequently administering a therapeutically effective amount of a GABA<sub>A</sub> receptor agonist and determining whether the subject is sensitive or insensitive to such GABA<sub>A</sub> agonist; and

(c) correlating a decreased sensitivity to a GABA<sub>A</sub> receptor modulator and an increased sensitivity to a GABA<sub>A</sub> agonist with an increased risk of premenstrual anxiety in the subject.

16. The method of claim 15 wherein the GABA<sub>A</sub> receptor modulator is a benzodiazepine.

17. The method of claim 15 wherein the GABA<sub>A</sub> receptor agonist is gaboxadol or THIP.

18. The method of claim 16 wherein the benzodiazepine is Valium (diazepam), Activan (lorazepam), Midazolam, or Flunitrazepam.

19. The method of claim 18 wherein the dose range is about 5-20 mg.

20. The method of claim 17 wherein the dose range is about 1-3 mg/kg.

21. A method of treating a subject at risk for premenstrual anxiety, said method comprising administering a therapeutically effective amount of a drug of claim 7, 8, or 9.

22. A drug which blocks  $\alpha_4\beta_2\delta$  GABA<sub>A</sub> receptors and identified by the method of claim 11, 12 or 21.

23. A method of treating a patient at risk for premenstrual anxiety, said method comprising administering a therapeutically effective amount of the drug of claim 11, 12 or 13.

24. The method of claim 8 or 12 wherein the eukaryotic cells are *Xenopus laevis* oocytes, Chinese hamster ovary (CHO) cells, mouse fibroblast L929 cells, mouse L(-tk) fibroblast cell line, human embryonic kidney cells, green monkey kidney cells, or COS cells.